closed population over a period of 3–5 months might have exerted a selection pressure over the circulating strains.

In the discussion section, 'access' is probably misprinted for 'assess'.

Comments on the rather low overall prevalence of *S. pyogenes*, and on the extraordinarily low one of *S. pneumoniae* – which cast doubts on the sensitivity of the isolation procedures – confusedly suggest, but do not admit, that the statistical power of the study was simply not adequate to draw conclusions.

Doubts also arise about the 'point prevalence snapshots', as the periods of training did not start and finish at single time points, given that the study was conducted 'between November 1994 and March 1995'; the actual date of the isolations should have been considered as a covariate.

The statement that the study was conducted in accordance with official guidelines is a poor substitute for the one usually required for clinical trials, and we remain with the disturbing doubt: has each study subject given a written and truly informed consent?

In conclusion, we much regret to see the official journal of the European Society of Clinical Microbiology and Infection accept as an Original Article a paper which is an untimely and incompetent manipulation of data already published. Needless to say, we would never advocate the mass use of azythromycin (or any other drug) to reduce streptococcal colonization in healthy adults.

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Response

We appreciate the authors' criticisms of our paper [1], but we wish to clarify some of their misunderstandings.

Our paper's [2] focus was rather simple. Using data from a previously published clinical trial [3], we sought to assess changes in antimicrobial susceptibility levels of two common respiratory pathogens (*Streptococcus pyogenes* and *S. pneumoniae*) among US military personnel enrolled in a respiratory disease chemoprophylaxis trial. Our findings, based upon limited data, indicated that there was little or no change in the minimum inhibitory concentrations (MICs) before and after the administration of the chemoprophylactic drugs.

We agree with Urbano and Urbano that using a single 1.2 million unit injection of benzathine penicillin G (BPG) injection is limited in its antimicrobial scope. We also recognize that the prophylactic effect of BPG against *S. pyogenes* is expected to protect an individual for only 2–4 weeks [4]. However, for more than 40 years, the US Department of Defense has successfully used mass BPG prophylaxis to prevent and control respiratory infection epidemics among military trainees [5–9]. This protection has been broad, frequently exceeding the magnitude of that which would be explained by the reduction of streptococcal infections alone [10]. The protection has also been prolonged, especially among US Army trainees, where a single dose of BPG will often protect a cohort for up to 8 weeks [10]. Although not well understood, the broad and persistent control is thought to be due to the impact mass BPG prophylaxis has on endemic respiratory pathogens in a training cohort as a whole. Such cohorts experience little mixing with other cohorts and benefit from a mass BPG influenced 'herd protection'.

As several 'outbreaks' of respiratory disease had occurred among US Marine trainees in Southern California in the late 1980s and early 1990s, the value of BPG interventions was questionable, considering the mixed etiology of infecting agents [11–13]. There was also concern that BGP prophylaxis might eventually select for penicillin-resistant/tolerant *S. pyogenes* strains and the US Department of Defense would be wise to identify alternative therapies. In contrast to Urbano and Urbano's comments, we believe the literature suggests that the threat of selecting for penicillin tolerance/resistance to be very real [14–16]. We were seeking an alternative antibiotic intervention with broad impact, for use in fast-moving respiratory epidemics. The aim of the original study [3] was to compare the efficacy of azithromycin with the then routine outbreak intervention of a single injection of BPG [9]. We compared the interventions for their protection against a number of respiratory pathogens.

We agree that the isolation procedure (throat swabs) for the recovery of both strains was not the optimal method and may have underestimated the true prevalence of both species among our trainees. However, the same method was used for

the pre- and post collection in all three treatment groups, and it is unlikely that a reduction in detection would have markedly changed our findings.

Finally, we agree with Urbano and Urbano that the statistical methods and analysis used in this study were not optimal, but they were adequate for the generalized MIC comparison between groups. Cross-sectional samplings were used under a simple pre- and post-treatment design and the results, with limited statistical power due to low prevalences, should be viewed as hypothesis-generating. We also agree that further chemoprophylaxis studies are merited to fully satisfy our observations that chemoprophylaxis with azithromycin did not appear to induce antibiotic resistance in either *S. pneumoniae* or *S. pyogenes*.

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